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Date: May 5, 2004 **Total pages:** 10

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Our Docket No.
Your Docket No. **Client/Matter No.** 078230/00031

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MESSAGE:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Philip John Burke and Richard John Knox

Serial No.: 10/099,830 Art Unit: 4061

Filed: March 13, 2002 Examiner: G. Nickol

For: *THERAPEUTIC SYSTEMS*

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($)

Complete if Known	
Application Number	10/099,830
Filing Date	March 13, 2002
First Named Inventor	Philip John Burke
Examiner Name	Gary B. Nickol
Art Unit	1642
Attorney Docket No.	ERD 100 CON

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 50-3129

Deposit Account Name: Pabst Patent Group LLP

The Director is authorized to: *(check all that apply)*

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☑ Charge any additional fee(s) or any underpayment of fee(s)

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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims	Fee from below	Fee Paid
Total Claims	3	-40* =	0	X	=
Independent Claims	1	-11** =	0	X	=
Multiple Dependent					=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid SUBTOTAL (3) ($)

SUBMITTED BY				(Complete *if applicable*)	
Name (Print/Type)	Patrea L. Pabst	*Registration No. (Attorney/Agent)*	31,284	*Telephone*	(404) 879-2151
Signature				*Date*	May 5, 2004

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PTO/SB/21 (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/099,830
Filing Date	March 13, 2002
First Named Inventor	Philip John Burke
Art Unit	1642
Examiner Name	Gary B. Nickol
Attorney Docket Number	ERD 100 CON

Total Number of Pages in This Submission

ENCLOSURES *(Check all that apply)*

- [✓] Fee Transmittal Form
- [ ] Fee Attached
- [ ] Amendment/Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
- [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Patrea L. Pabst, Esq., Reg. No. 31,284 Pabst Patent Group LLP 400 Colony Square, Suite 1200, Atlanta, GA 30361
Signature	
Date	May 5, 2004

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I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Typed or printed name	~~Hershey Miller~~ Patrea Pabst		
Signature		Date	May 5, 2004

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Serial No.: 10/099,830 Art Unit: 4061

Filed: March 13, 2002 Examiner: G. Nickol

For: *THERAPEUTIC SYSTEMS*

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO RESTRICTION REQUIREMENT

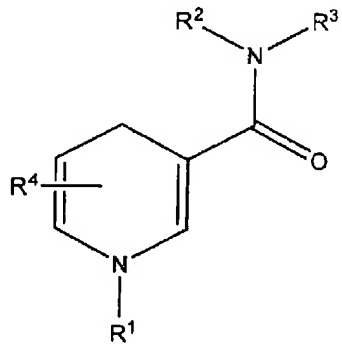
Sir:

Responsive to the Restriction Requirement mailed on April 5, 2004, please consider the following remarks. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

In the Claims

Claims 1-33 (Canceled).

34. (Currently amended) A ~~therapeutic~~ system comprising a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2 and ~~nicotinamide riboside (reduced) (NRH) or an analogue thereof which can pass reducing equivalents to NQO2~~ a compound of formula I

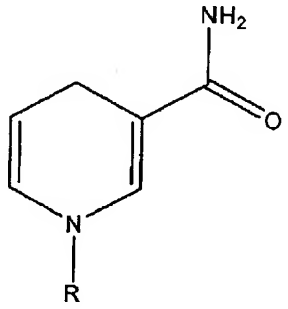


wherein R^1 is selected from the group consisting of substituted alkyl, including substitution by $CONH_2$, OH, halogen, CN, and COOH; aryl; substituted aryl; $CONR^aR^b$, where $R^a$and R^b are independently H, alkyl, or substituted alkyl, and R^2 and R^3 are independently H, alkyl, or substituted alkyl and R^4 is any of H, alkyl, substituted alkyl, halogen, CN, COOH, $CONH_2$, or OH, wherein the compound can pass reducing equivalents to NQO2, in a form for administration to a patient in need thereof.

Claims 35-40 (Canceled)

41. (Currently amended) The ~~method~~ system of claim ~~29~~ 34, wherein the ~~analogue of NRH~~ compound is 1-(carboxamidomethyl)-dihydronicotinamide.

42. (New) The system of claim 34, wherein the compound has formula II



wherein R is a substituted alkyl, comprising one or more groups selected from the group consisting of CNH_2, OH, halogen, CN, and COOH.

44. (New) The system of claim 34, wherein the alkyl group is a C_1 to C_6 alkyl.

45. (New) The system of claim 34, wherein R is selected from the group consisting of -CH_2CONH_2, -$CH_2CH_2CH_2SO_3^-$, -$CH_2CH_2CH_2OH$, and –CH_2CH_2COOH.

46. (New) The system of claim 34 wherein the analogue of NRH is 1-(carboxamidomethyl)-dihydronicotinamide.

Remarks

Restriction Requirement

In the Office Action mailed April 5, 2004, the claims were divided into fifteen (15) groups, as follows:

Group 1, claims 1-7 and 24, drawn to compound comprising a target cell-specific portion and human NAD(P)H:quinine reductase 2 (NQO2);

Group 2, claims 1-7, 12, and 24, drawn to a compound comprising a target cell-specific portion and a polynucleotide encoding NQO2, variant, fragment, fusion, or derivative;

Group 3, claims 8-11, drawn to a recombinant polymnucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2;

Group 4, claims 13-17, drawn to a therapeutic system comprising a protein compound comprising a target cell-specific portion and human NAD(P)H:quinine reductase 2 and a prodrug;

Group 5, claims 13-17, drawn to a therapeutic system comprising a polynucleotide encoding NQO2, a target cell-specific portion, and a prodrug;

Group 6, claims 18-23, drawn to a method of treating a patient with a target cell to be destroyed comprising administering a protein compound comprising a target cell-specific portion and human NAD(P)H:quinine reductase 2;

Group 7, claims 18-23, drawn to a method of treating a patient with a target cell to be destroyed comprising administering a recombinant polynucleotide, comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2;

Group 8, claims 25 and 26, drawn to use of a protein compound comprising a target cell-specific portion and human NAD(P)H:quinone reductase 2;

Group 9, claims 25 and 26, drawn to use of a recombinant polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2;

Group 10, claims 29, 31-33, 40 and 41, drawn to a method of treating a human patient with a target cell to be destroyed comprising administering CB1954 and NRH or an analogue thereof;

Group 11, claim 34, drawn to a therapeutic system comprising a prodrug and nicotinamide riboside;

Group 12, claim 35, drawn to nicotinamide riboside (NRH) or an analogue thereof;

Group 13, claims 36 and 37 drawn to use of NRH in the manufacture of a medicament for treating a human patient with a target cell to be destroyed;

Group 14, claims 27, 28, and 38, drawn to use of a prodrug; and

Group 15, claim 39, drawn to a kit comprising a means for determining whether a target cell to be treated expresses NQO2 and NRH or an analogue thereof which can pass reducing equivalents to NQO2.

This application is a continuation of U.S.S.N. 09/445,865 filed February 11, 2000, now allowed. The parent application was subject to a restriction requirement on February 13, 2001. ***The same claims are presented in this application yet have been subjected to a different restriction requirement by the same examiner.*** On this basis alone, the undersigned must traverse the restriction requirement. For example, claims 13-17 were previously divided into three groups (this restriction was traversed) – now they are divided into two groups; claim 32

was previously placed into group 12; now it is placed into group 10 with a different set of claims. This makes it impossible to determine what the examiner believes the different inventions to be.

To the extent one can make an election, applicants elect to prosecute the invention of claim 34, group 11.

Claims 1-33 and 35-40 have been canceled, without prejudice with the understanding that these claims can be prosecuted in later filed applications. Claim 41 has been amended to depend from claim 34, which as been amended to refer to a compound of formula I. New claims 42-46 have been added. Support for the new claims are found in the specification at least at page 49, line 25 to page 50, line 7 and page 51, lines 7-8; page 50, line 12 to page 51, line 1; page 51, line 4; page 51, lines 10-22; and page 46, lines 7-9.

Election of Species

Groups 1 and 2 were further classified by species: a) an antibody or fragment or derivative, and b) macromolecule. The election of species is moot since these claims have been canceled.

No change in inventorship is required by virtue of the response to restriction requirement.

Issuance of an office action on the merits of claims 34 and 41, as amended, and new claims 42-46 is respectfully solicited.

Respectfully submitted,

Patrea L. Pabst
Reg. No. 31,284

Date: May 5, 2004

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Certificate of Facsimile Transmission

I hereby certify that this Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on this date, May 5, 2004, to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Patrea L. Pabst

Date: May 5, 2004